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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/565,065

01/17/2006

Eddy Jean Edgard Freyne

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EXAMINER

MURRAY, JEFFREY H

ART UNIT

PAPER NUMBER

1624

NOTIFICATION DATE

DELIVERY MODE

01/07/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@woodcock.com

Office Action Summary	Application No. 10/565,065	Applicant(s) FREYNE ET AL.	
	Examiner JEFFREY H. MURRAY	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 October 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-14 and 19 is/are allowed.
- 6) ☒ Claim(s) 15-18 and 20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/10/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Claims

1. Claims 1-14 and 18 are rejected. Claims 15-17, 19 and 20 are withdrawn.
2. Claims 14, 20-22, 24 and 25 are pending in this application. Claims 15-19 and 23 have been cancelled. This action is in response to the applicants' amendment after a non-final and reply filed on August 20, 2007.

Status of Objections

3. The specification was objected to as not containing a proper Abstract of the Disclosure. The objection to the specification is hereby withdrawn in view of applicants' amendments to the specification.
4. Claims 1 and 12 were objected to as containing minor informalities. The objection to the claims is hereby withdrawn in view of applicants' amendments to the claims.

Status of Rejections

5. Claims 1-14 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to meet the enablement requirement. The rejection of Claims 1-14 and 18 are hereby withdrawn in view of applicants' arguments being persuasive.
6. Claims 1, 12, and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite. The rejection of Claims 1, 12 and 13 are hereby withdrawn in view of applicants' amendments to the Claims.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

Election/Restrictions

7. Claims 1-14 are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(B), claims 15-17, 19, and 20, directed to the process of making or using an allowable product, previously withdrawn from consideration as a result of a restriction requirement, are hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Because all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, the restriction requirement as set forth in the Office action mailed on May 15, 2007 is hereby withdrawn. In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

New Rejections

Claim Rejections - 35 USC § 112, 1st paragraph

8. Claims 15-17 and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds and compositions, does not reasonably provide enablement for N-oxides of any of the compounds or compositions or does it teach how to “prevent” the various diseases listed in the claims. The

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specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

9. The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation. (*United States v. Teletronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors (See *Ex parte Forman* 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988)).

These factors include the following:

1) *Unpredictability in the art.* Triazolopyrimidines are currently available drugs for treating depression (antidepressants) such as trazodone; however, tricyclic or similar cyclic anti-depressants have been shown to have side effects such as anticholinergic effects (dry mouth, blurred near vision, constipation, dysuria), antihistamine effects (weight gain, sedation), antiadrenergic effects (postural hypotension, vertigo, dizziness) and cardiotoxicosis or acute poisoning caused by excessive intake. (Nishibe, et. al. US 6,737,085).

The use of the term “prevention” is, unless otherwise defined, interpreted to mean inhibition of pain and inflammation once the active agent has been administered. Applicant must show that the Claimed method “prevents” pain and inflammation in a broad range of conditions. The specification fails to enable the claimed compounds for

the prevention of pain and inflammation. The term “prevention” encompasses the ability of the specific antigen to induce protective immunity to any inflammatory disorder. For example, multiple sclerosis or MS represents an unpreventable chronic illness.

(Schiaffino et. al., *J.Behav.Med.*, 1995, 18(6), p.536) Chronic neurological pain is the most common and the most intractable of the pain syndromes of MS.

(<http://www.msakc.org/Articles/MSPain.htm>). In view of the situation set forth herein, it is clear that it is not possible for the instant compounds or compositions to “prevent” pain and inflammation commensurate in scope with Claim 15 and 16.

The specification does not provide sufficient data or provide substantive evidence that the claimed compounds are capable of inducing protective immunity against disease and disorders broadly. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed compound, i.e. would not be able to accurately predict if a disease or disorder had been prophylaxed.

The applicants have broadly labeled diseases and disorders that they believe the inhibition of a GSK3 or JNK3 protein kinase will treat. However even the names of the disorders are so broad that one skilled in the art cannot determine what is meant. For example, the term “diabetes” is ambiguous. It is not a complete term. Diabetes insipidus for example is caused by the inability of the kidneys to conserve water, which is caused by a lack of ADH (central diabetes insipidus) or by failure of the kidneys to respond to ADH (nephrogenic diabetes insipidus). Applicants must select some specific form(s) of diabetes (e.g. Type 2 diabetes mellitus, maturity-onset diabetes of the young

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(MODY, which comes in 6 completely different forms arising from different genetic defects), Gestational diabetes mellitus (“GD”) and neonatal diabetes, which also arises from a specific genetic defect; these are metabolic disorders) and they must use that term, and show that one of ordinary skill in the art would have been able to determine that whatever term(s) is/are selected was the one(s) intended.

The term “inflammatory diseases” is vague and indefinite making treating the disease unpredictable. By itself, it is not a standard medical term for a specific disease or groups of related diseases, but a general term. For example, arthritis can denote inflammation of the joints, and may or may not involve inflammation of other parts of the body such as the nails. It mostly commonly refers to any of osteoarthritis, gouty arthritis, or rheumatoid arthritis. These are three totally different and unrelated inflammatory disorders, which all have “arthritis” in their name and involve inflammation of the joints. Rheumatoid arthritis is an inflammatory disorder causing destruction of articular cartilage. It is an autoimmune condition where the body's immune system attacks its joints. In gouty arthritis, joint inflammation is caused by the formation of monosodium urate monohydrate (MSU) crystals within the joint space. Osteoarthritis is a degenerative cartilage disorder; cartilage breakdown causes bones to rub against each other. Causes include injuries, diseases such as Paget's disease, and long-term obesity, but often the cause is unknown.

Another example would be cancer. While the state of the art is relatively high with regard to the treatment of specific cancer types, the state of the art with regard to treating cancer broadly is underdeveloped. The Cecil reference (Cecil Textbook of

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Medicine, 21st Edition (2000), Goldman & Bennett (Editors), W.B. Saunders Company (Publisher), Chapter 198, pages 1060-1074) clearly shows that for the various known cancer types, there is no one specific chemotherapeutic agent that is effective for all types of cancer (see page Table 198-5 at page 1065; Tables 198-6 and 198-7 at page 1066; Table 198-8 at page 1068; and Table 198-9 at page 1071). The cancer therapy art remains highly unpredictable, and no example exists for efficacy of a single product against tumors generally. Specifically, Internal Medicine, 4th Edition, Editor-in-Chief Jay Stein, Chapters 71-72, pages 699-715, teaches that the various types of cancers have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocol.

2) *Amount of guidance provided by Applicant.* Applicant has provided no guidance or examples of any N-oxide derivatives of the compounds or compositions. Applicants have also not provided any guidance, examples, or provided any biological data and/or testing results of “preventing” any of the various diseases listed, only that these compounds and compositions have an effect on the GSK3b assay.

3) *Number of working examples.* Applicant has provided no working examples of any N-oxides or a compound or composition that can “prevent” the diseases or disorders in the present application.

4) *Nature of the invention.* The nature of this invention concerns a novel group of compounds, their use as a medicine, their use for the manufacture of a medicament for the treatment of diseases mediated through glycogen Synthase kinase 3 (GSK3), in

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particular glycogen synthase kinase 3 α and 3 β ; processes for their preparation and pharmaceutical compositions comprising them.

5) *Level of skill in the art.* The artisan using Applicants invention would be a chemist with a M.S. or Ph.D. degree, and having several years of bench experience or a doctor with an M.D. degree, and having several years of experience.

MPEP §2164.01 (a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here that Applicant is not enabled for making these compounds or compositions.

Claim Rejections - 35 USC § 112, 2nd paragraph

10. Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. The term "therapeutically effective amount" in Claim 18 is a relative term which renders the claim indefinite. The term " therapeutically effective amount " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

The term "therapeutically effective amount" in Claim 18 cannot be defined because there is no disorder or disease mentioned within the claim. How can one administer a "therapeutically effective amount" when no mention is made of what disease or disorder is being treated? Examiner suggests removing the words "a therapeutically effective amount" from the Claim. Appropriate correction is necessary.

Allowable Subject Matter

12. Claims 1-14 and 19 are allowed.

Claims 1-14 and 19 are allowed because no prior art reads on the current application's claims. Gillespie, et al. (WO 2002/055082) teaches compounds that are similar in scope to the compounds in the current application. However, Gillespie et. al. fails to teach triazolopyrimidines with the proper substituent groups, it teaches pyrazolopyrimidines with the appropriate substituent groups.

Conclusion

13. Rejoined Claims 15-18 and 20 are rejected.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is 571-272-9023. The examiner can normally be reached on Mon.-Thurs. 7:30-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey H Murray/

/James O. Wilson/

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